REMARKS

Favorable reconsideration of this application as presently amended and in light of the following discussion is respectfully requested.

Claims 1-17 are pending in the present application. In the present Request for Reconsideration, none of the claims are amended.

In the December 7, 2009 Office Action, Claims 1-9, and 11-12 were rejected as unpatentable under 35 U.S.C. § 103(a) over the reference Lindsay et al. (U.S. Patent Publication No. 2004/0238379, hereinafter "Lindsay") in view of Kariyone et al. (U.S. Patent No. 5,242,793, hereinafter "Kariyone"), in further view of Hafeman et al. (U.S. Patent No. 5,164,319, hereinafter "Hafeman"). Claim 10 was rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone and Hafeman, in further view of Hashimoto (U.S. Patent Publication No. 2001/0024788). Claim 13 was rejected as unpatentable under 35 U.S.C. § 103(a) over the reference Lindsay in view of Kariyone and Hafeman, in further view of Price (U.S. Patent No. 5,805,014). Claims 14-15 were rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone and Hafeman, in further view of Hollis et al. (U.S. Patent No. 5,653,939, hereinafter "Hollis"), Dryja et al. (U.S. Patent No. 5,498,521, hereinafter "Dryja".) and Blackburn (U.S. Patent Application No. 2003/0190608).

Moreover, Claims 14 and 16 were rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone and Hafeman, in further view of Hollis et al. (U.S. Patent No. 5,653,939, hereinafter "Hollis"), Sorenson (U.S. Patent No. 5,496,699) and Blackburn. Claim 17 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Lindsay, in view of Kariyone and Hafeman, in further view of Anderson et al. (U.S. Patent No. 5,922,591, hereinafter "Anderson"). Claim 18 was rejected under 35 U.S.C. § 103(a) as

being unpatentable over Lindsay, in view of Kariyone, in further view of Heller et al. (U.S. Patent No. 6,281,006, hereinafter "Heller").

In response to the rejection of Claims 1-9, and 11-12 under 35 U.S.C. § 103(a), Applicants respectfully request reconsideration of this rejection and traverse the rejection, as discussed next.

Briefly summarizing, Applicants' Claim 1 is directed to a method for detecting at least one parameter representative of molecular probes fixed to active zones of a sensor, wherein said sensor includes a network of field-effect transistors, each of which has a source region, a drain region, and a gate region which forms one of said active zones on which said representative parameter is detected. The method includes the following steps: (a) bringing some of said active zones into contact with molecular probes in order to fix said probes; (b) bathing at least some of said active zones which have been brought into contact with said molecular probes, in an electrolyte solution; (c) measuring at least one point of at least one of a drain current, source-gate voltage, and source-drain voltage characteristic of at least two of the field-effect transistors having at least two active zones that are part of some of active zones, corresponding to a first group, so as to deduce therefrom the representative parameter by comparison between at least two measurements obtained for two different active zones immerged in the electrolyte solution; and (d) fixing a potential of the electrolyte solution which covers the active zones with an electrode that applies a gate source voltage to the field effect transistors, the electrode being immerged in the electrolyte solution.

Applicants respectfully traverse the obviousness of the combination of Lindsay and Karione. The pending Office Action asserted that the combination of these references is obvious for one of ordinary skill in the art, and provided the following reasoning for the obviousness:

> The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a method having the added advantage of ***providing a quality control indicator for each of the sensors*** of the method as a result of confirming the stable immobilization of the probe to the surface as explicitly taught by Kariyone et al. (column 17, lines 1-10). In addition, it would have been obvious to the ordinary skilled artisan that the known technique of using the initial detection of the immobilization of a probe as taught by Kariyone et al could have been applied to the method of Lindsay et al with ***predictable results*** because the known technique of using the initial detection of the immobilization of a probe as taught by Kariyone et al predictably results in verification of stably immobilized probes.

(Office Action, p. 5, ll. 3-12, emphasis added.) Applicants traverse this reasoning for that has been provided for the obviousness, as next discussed.

First, Lindsay is directed to a method for electronically detecting hybridization of a probe nucleic acid and a target nucleic acid. (Lindsay, Abstract.) For his method, Lindsay explains that a back-gated field effect transistor FET is used, where a layer of silicon 10 is provided on a buried oxide layer 20, located on a silicon wafer or substrate 30, where a source 40 and drain 50 and a n-channel 65 are provided in the silicon 10. (Lindsay, p. 2, ¶¶ [0019]-[0020], Fig. 1a.). A fluid placed on or in an upper surface 75 of n-cannel 65 the semiconductor can be charged to interact with the semiconductor. (Lindsay, p. 3, ¶ [0028], Figs. 1a, 1b). Lindsay also explains that when the FET is operated with a buffer including a DNA on the channel 65 for a measurement, an applied drain-source bias voltage 70 is kept constant, and a backgate voltage 60 V_{bg} is grounded, so that his silicon wafer or substrate 30 is also grounded. (Lindsay, p. 4, ¶ [0036]-[0037], Fig. 7.) In other words, as can be seen from Lindsay's Figure 2, the gate voltage of Lindsay's FET is floating. In light of this configuration of Lindsay's FET, it is *not possible* to fix both the potential of the fluid, for example the non-hybridizing target DNA, and the gate voltage, so that it will be the same for all the FET transistors used. (See Lindsay, ¶¶ [0035]-[0037]). In addition, the reference Lindsay makes no suggestion how to fix both the potential of the fluid and the gate of the FET.

In contrast, the reference Kariyone is directed to capacitively operated electrodes that generate electrical fields, having an electrically conductive base, and a selectively permeable membrane which is produced by forming a membrane from a mixed solution comprising (a) albumin, (b) at least one type of cross-linking agent and (c) chitosan. (See Kariyone, Abstract.) The electrode is used to detect consumption of oxygen or formation of hydrogen peroxide in biochemical reactions by an immobilized enzyme. (Kariyone, col. 1, ll. 56-60.) In order to avoid the detection of other substances, such as ascorbic acid, Kariyone explains that a selective permeable membrane can be placed between the immobilized enzyme and the hydrogen peroxide electrode. (Kariyone, col. 1, l. 64, to col. 2, l. 4.) Moreover, Kariyone has a solution that can enhance strength of the selective permeable membrane, by using a cross-linking agent to fix the enzyme, a globular protein, and a high molecular substance. (Kariyone, col. 3, l. 62, to col. 4, l. 7.)

Regarding Kariyone's measurement system, it is explained that a working electrode E1-E6 used together with comparison electrodes C1-C6 to detect redox reaction, and a counter electrode 7 can balance the electrons added or removed by the working electrodes E1-E6, and a reference electrode 8 that controls the working electrodes E1-E6 potential. (See Kariyone, col. 9, ll. 2-28, Fig. 1.) To perform the measurements with electrodes E1-E6 and C1-C6, Kariyone explains that that these electrodes are *not used simultaneously*, but are used from one experiment to the next. (See Kariyone, examples, from col. 9 to col. 17.) In particular, twelve successive experiments are performed in Kariyone. Therefore, Kariyone fails to teach any differential measurements that are performed between respective electrodes E1-E6 and C1-C6. Kariyone also does not use any transistors to perform his measurements, but applies electrical fields between two electrodes. (Kariyone, col. 9.)

In light of these substantial different measurement principles of Lindsay and Kariyone, where Lindsay is directed to a measurement system using a FET device, where

fluids are placed on a channel region and a threshold voltage is detected, and Kariyone is putting immobilized enzymes between two electrodes E1-E6 and C1-C6, it is believed that combination is not obvious. Applicants' traverse the reasoning that the ordinary artisan would have been motivated to make such modification because said modification "would have resulted in a method having the added advantage of providing a quality control indicator for each of the sensors." (Office Action, p. 5, ll. 3-7.) The measurement devices of both Lindsay and Kariyone are based on totally different measurement principles, and the reference electrode 8 shown in Kariyone's Figure 1 cannot be readily included into Lindsay's field effect transistor FET. In addition, there is absolutely no reasoning or proof that the introduction of a reference electrode 8 into Lindsay's field effect transistor would actually provide "a quality control indicator for each of the sensors," as proclaimed in the Office Action, and a substantial redesign of Lindsay's FET and his measurement method may be required. *See In re Ratti*, 270 F.2d 810, 813, 123 USPQ 349, 352 (reversing an obviousness rejection where the "suggested combination of references would require a substantial reconstruction and redesign of the elements shown in [the primary reference] as well as a change in the basic principle under which the [primary reference] construction was designed to operate.") Please note that the decision of *In re Ratti* was not reversed by the decision *KSR v. Teleflex*, 550 U.S. 398 (2007).

In addition, it is believed that the references, Lindsay and Kariyone in light of the above discussion, are non-analogous art. To use two rejection references and to combined them to find obviousness, the U.S.P.T.O. has to find that there are some structural similarities and functional overlap of both references. See M.P.E.P. 2141.01(a). See also *In re Ellis*, 476 F.2d 1370, 1372, 177 USPQ 526, 527 (CCPA 1973). However, in this case the measurement principles of Lindsay and Kariyone are substantially different. In addition, the reference Lindsay teaches a field effect transistor that is operated based on purely electrical technology,

(see i.e. Lindsay, ¶ [0010], measuring shift in threshold voltage) where Kariyone is based on electrochemical reactions. (see i.e. Kariyone, col. 10, ll. 1-11, detecting measurement currents based on ascorbic acids.) Therefore, a person of ordinary skill in the art would not readily combine Kariyone's reference electrode 8 made of a special metal to apply a reference potential (Kariyone, col. 9, ll. 9-10) into Lindsay's FET that has to detect a threshold voltage. Under such combination, it is possible that Lindsay's FET does not even operate any more. Therefore, it is believed that both references are not analogous art, and Applicants also believe that the suggested combination does *not* lead to "predictable results because the known technique of using the initial detection of the immobilization of a probe as taught by Kariyone et al predictably results in verification of stably immobilized probes" as reasoned by the pending Office Action. (See Office Action, p. 5, ll. 7-12.)

Moreover, Applicants also respectfully traverse the reasoning for the obviousness to combine the reference Hafeman with the Lindsay's FET. The pending Office Action stated that it would have been obvious to combine Hafeman's use of electrodes in pixel elements to detect an analyte in a fluid into Lindsay's FET. (See Office Action, p. 6, ll. 3-19.) Applicants respectfully traverse this reasoning and the rejection, as next discussed.

Hafeman is not directed to any field-effect transistors, but is directed to a capacitively operated device for detecting particles having an electrode 10 and a counter-electrode 14. (Hafeman, Abstract, Fig. 1.) His electrode 10 is made of a substrate that has doped semiconductor material, for example n type of p type, with regions or "pixels" that are electrically isolated from each other. Moreover, in Hafeman, these regions can be similarly doped, or oppositely doped, and when they are similarly doped, there will be a positively doped barrier 17 separating each of the regions from each other. (Hafeman, from col. 14, l. 65 to col. 15, l. 1.) In addition, Hafeman's electrode 10 is coated with an uniform insulating layer and the particle detection is done by measuring the capacitance between the electrodes

10 and 14. Regarding measurement principles that use field-effect transistors, like Lindsay's method, Hafeman explains the following:

> The FET devices have not found commercial acceptance and in many sitations, lack flexibility. For use as chemical detectors, FET devices particularly suffer from the difficulty of obtaining exposed gate regions and working with them in an experimental environment.

(Hafeman, col. 1, ll. 31-36.) In other words, a person of ordinary skill in the art would not use Hafeman's electrodes 10, 14 of a capacitor to make capacitive measurements, and introduce them into Lindsay's FET that has a drain-source bias voltage 70 that is kept constant, and a gate that is floating. Therefore, not only can the features of Hafeman not readily be combined into Lindsay's FET, but also Hafeman clearly teaches away from Lindsay's solution. In this respect, the case law sets forth that a reference may be said to teach away when a person of ordinary skill in the art, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by an applicant. *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

Should the Examiner continue to disagree with the above distinctions, Applicants respectfully request that the Examiner provide an explanation via Advisory Action pursuant to M.P.E.P. § 714.13 specifically rebutting the points raised herein for purposes of facilitating the continued prosecution or an appeal process.

Consequently, in view of the present request for reconsideration, no further issues are believed to be outstanding in the present application, and the present application is believed to be in condition for formal Allowance. A Notice of Allowance for Claims 1-17 is earnestly solicited.

Should the Examiner deem that any further action is necessary to place this application in even better form for allowance, the Examiner is encouraged to contact Applicants' undersigned representative at the below listed telephone number.

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